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said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of an enzyme in said enzyme family, to form a module;

(b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;

(c) screening said population of bi-ligands for binding to an enzyme in said enzyme family;

(d) identifying a bi-ligand that binds to and has specificity for said enzyme; and

(e) repeating steps (c) and (d) to identify a bi-ligand that binds to and has specificity for a second enzyme in said enzyme family.

11. The method of claim 9, wherein said enzyme in said enzyme family is an enzyme selected from the group consisting of a kinase, dehydrogenase, oxidoreductase, GTPase, carboxyl transferase, acyl transferase, decarboxylase, transaminase, racemase, methyl transferase, formyl transferase, and α -ketodecarboxylase.

12. The method of claim 9, wherein said enzyme family binds a cofactor selected from the group consisting of nicotinamide adenine dinucleotide, nicotinamide adenine dinucleotide phosphate, thiamine pyrophosphate, flavin adenine

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dinucleotide, flavin mononucleotide, pyridoxal phosphate, coenzyme A, tetrahydrofolate, adenosine triphosphate, guanosine triphosphate and S-adenosylmethionine.

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ant
13. The method of claim 9, wherein said linker has approximate C2 symmetry.

14. The method of claim 13, wherein said linker has perfect C2 symmetry.

D3
137. The method of claim 9, wherein steps (c) and (d) are repeated to identify a bi-ligand that binds to and has specificity for a third enzyme in said enzyme family.

α Please add the following new claims. β

38. (New) A method for identifying a population of bi-ligands to enzymes in an enzyme family, comprising:

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(a) attaching a linker to a common ligand, wherein said common ligand competes for cofactor binding, wherein said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of an enzyme in said enzyme family, to form a module;

(b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;

(c) screening said population of bi-ligands for binding to an enzyme in said enzyme family;

(d) identifying a bi-ligand that binds to and has specificity for said enzyme; and

(e) repeating steps (c) and (d) to identify a bi-ligand that binds to and has specificity for a second enzyme in said enzyme family.

39. (New) The method of claim 38, wherein said expansion linker has approximate C2 symmetry.

40. (New) The method of claim 38, wherein said expansion linker has perfect C2 symmetry.

41. (New) A method for identifying a population of bi-ligands to enzymes in an enzyme family, comprising

(a) attaching a linker to a common ligand, wherein said common ligand is a cofactor or mimic thereof and wherein said linker has sufficient length and orientation to direct a second ligand to a substrate binding site of an enzyme in said enzyme family, to form a module, wherein said enzyme family comprises two or more enzymes that bind to the same cofactor;

(b) generating a population of bi-ligands, wherein said bi-ligand comprises said module and a second ligand linked by said linker;